REMARKS

This submission is a response to the Office Action dated June 13, 2005, (hereinafter the "Office Action"). Claims 1, 5-6 have been amended. Claims 1-7, 9-20 and 38-41 remain pending. Claim 1 has been amended to narrow the claim by deletion of some of the antioxidants.

Rejections under 35 U.S.C. §112

Claims 5-6 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite on the basis of the use of the terms, "comprises" in these claims. Claims 5-6 have been amended in order to remove the word, "comprises" thereby obviating the rejection. Favorable consideration and withdrawal of the rejection of claims 5-6 is requested in view of these amendments.

Provisional Double Patenting Rejections

Claims 1, 4-9 and 12-20 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of copending application no. 10/288,761, and claims 1-25 of copending application no. 10/279,315. The applicant would like to defer response to these provisional rejections until such time as claims of either copending application no. 10/288,761, or copending application no. 10/279,315, are indicated as being allowable.

Rejections under 35 U.S.C. § 103(a)

Claims 1-4, 7, 9-20, 38 and 42 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,162,801, issued to Kita (hereinafter "Kita"), Bissett, D.L. *et al.*, *J. Soc. Cosmet. Chem.* **1992**, *43*, 85-92 (hereinafter "Bissett"), and Darr, D. *et al.*, *British Journal of Dermatology* **1992**, *127*, 247-253 (hereinafter "Darr"), in view of Shimoi, K., *et al.*, *Mutation Research* **1996**, *350*, 153-161 (hereinafter "Shimoi") and U.S. Patent No. 5,776,460, issued to Kim et al. (hereinafter "Kim"). Applicant respectfully traverses this rejection for the reasons set forth below.

Applicant respectfully submits that the Official Action does not set forth a *prima facie* case of obviousness in support of the rejection under 35 U.S.C. § 103(a). According to M.P.E.P. § 2143,

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.
>
> The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. [*Citation omitted.*]

As discussed in detail in the Amendment After Final Rejection filed on January 24, 2005, none of the references relied upon by the Examiner in support of the rejections under 35 U.S.C. §103(a) discloses:

(1) administration of D vitamins for the purpose of treating radiation injury resulting from proton radiation, fluoroscopic radiation, alpha radiation, beta radiation and gamma radiation, or

(2) use of either D vitamins or the antioxidants of claim 1 to treat radiation injury resulting from proton radiation, fluoroscopic radiation, alpha radiation, beta radiation and gamma radiation.

Applicant submits that the cited references do not contain every element of a *prima facie* case of obviousness, since at least these two elements of claim 1 are missing from the cited references and all of the dependent claims currently pending in the present application ultimately depend from independent claim 1. Accordingly, Applicant submits that the Official Action does not set forth a *prima facie* case for the obviousness of any pending claim of the present application over the cited references.

In addition, the cited references also do not set forth a case of *prima facie* obviousness because the cited references provide no teaching or suggestion that would provide a skilled person with an expectation of successfully treating radiation injury from one of the types of radiation claimed in claim 1, by oral administration of a composition including vitamin D_3.

Therefore, for this additional reason, the cited references do not set forth a case of *prima facie* obviousness.

Further, in support of the obviousness rejection, the Examiner relies on the following motivation to combine the teachings of the numerous references relied upon:

> "Furthermore, as indicated in the previous Office Action, since all active composition components herein are known to [be] useful to treat radiation injury, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980)." Final Rejection at page 12.

However, this motivation cannot be sustained since it is inconsistent with a previous position taken by the Examiner wherein the Examiner stated that,

> "It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity." Office Action dated April 30, 2004, page 5. (emphasis original)

Thus, on April 30, 2004, the Examiner took the position that due to the unpredictability of the pharmaceutical art, each embodiment or combination of ingredients must be individually assessed for physiological activity. However, the Examiner now takes the position that a skilled person would expect at least additive therapeutic effects for each embodiment. This is clearly inconsistent with the Examiner's earlier position, since the Examiner took the earlier position that is not possible for the skilled person to expect any specific therapeutic effect of a particular embodiment, since the pharmaceutical art is highly unpredictable and each combination of ingredients must be individually assessed for physiological activity. Accordingly, by the Examiner's own earlier admission, there is no motivation for a skilled person to combine the ingredients of the various cited references since, as the Examiner stated in the April 30, 2004, Office Action, the skilled person cannot predict the physiological activity of such combinations without individually assessing the physiological activity of each combination. Therefore, the skilled person would not have an expectation of success for combinations of the ingredients and thus no motivation to combine them.

Finally, the Examiner stated that, "... the record contains no clear and convincing evidence of nonobviousness or **unexpected results** for the oral compositions herein employed in

the claimed method herein over the prior art." (emphasis original) See page 12 of the Final Rejection.

In response to this comment, the applicant has submitted the Declaration of Gerald H. Sokol, M.D., which provides evidence of nonobviousness and/or unexpected results for the compositions as specified in the pending claims. More specifically, the Declaration shows that compositions in accordance with the present invention, when administered to mice prior to, on the day of, and/or after exposure to ionizing radiation, provided clinically and statistically significant improvements in the percentage survival of these mice, relative to control mice that received the vehicle only, without the active ingredients.

These results are clearly unexpected since none of the prior art references cited by the Examiner contains any teaching or suggestion that administration of a composition in accordance with the method of the present invention would increase survival rates of any living creature exposed to ionizing radiation. Thus, there is no evidence of record that a skilled person would expect that administration of such compositions would provide this result. Therefore, the result is unexpected.

The Examiner alleges that the declaration of Dr. Sokol is insufficient for two reasons:

(1) the examples are not commensurate in scope with the claims, and

(2) that the applicant has not compared the invention to the closest prior art.

The first issue is a non-issue, since the only evidence of record relating to the performance of the claimed method is the Declaration of Dr. Sokol. Thus, the Examiner has presented no evidence that the results of the Declaration of Dr. Sokol would not apply over the entire claimed subject matter, nor has the Examiner given a plausible reason, supported by evidence, as to why the evidence would not be expected to apply over the entirety of the claimed subject matter.

The second issue appears to the applicant to also be a non-issue since none of the prior art relied on by the Examiner even relates to the same purpose as the present invention. Specifically, none of the prior art relied on by the Examiner relates to treatment of a human or animal exposed to proton radiation, fluoroscopic radiation, alpha radiation, beta radiation and gamma radiation. Thus, assuming that Kita represents the closes prior art, the Examiner appears to be advocating that the applicant topically apply vitamin D to the skin of an animal and expose that animal to lethal doses of proton radiation, fluoroscopic radiation, alpha radiation, beta

radiation and gamma radiation in order to prove that topical application of vitamin D does not provide treatment of radiation injury. This seems to be an waste of laboratory animals since the applicant can already predict that topical application of vitamin D will not work since vitamin D does not absorb significant amounts of proton radiation, fluoroscopic radiation, alpha radiation, beta radiation and gamma radiation. It is not understood how such testing would be relevant to the patentability of the present invention.

In this regard, the Examiner must bear in mind that although evidence of unexpected results must compare the claimed invention with the closest prior art, applicant is not required to compare the claimed invention with subject matter that does not exist in the prior art. *In re Geiger*, 815 F.2d 686, 689, 2 USPQ2d 1276, 1279 (Fed. Cir. 1987) (Newman, J., concurring) (Evidence rebutted *prima facie* case by comparing claimed invention with the most relevant prior art. Note that the majority held the Office failed to establish a *prima facie* case of obviousness.); *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966) (Requiring applicant to compare claimed invention with polymer suggested by the combination of references relied upon in the rejection of the claimed invention under 35 U.S.C. 103 "would be requiring comparison of the results of the invention with the results of the invention." 357 F.2d at 422, 148 USPQ at 714.).

Thus, the closest prior art is so far away from the present invention, as explained above, that there can be no meaningful comparison of the prior art to the claimed invention. Rather, the applicant has merely provided additional evidence, in the form of the declaration of Dr. Sokol, to support nonobviousness by demonstrating that compositions of the present invention provide meaningful radiation protection in mice. However, this evidence is not even necessary, since, as discussed above, the Examiner has not presented a case of *prima facie* obviousness since several elements of the claimed invention are lacking from the cited prior art.

The Examiner alleges that because the UV radiation molar absorption coefficients for vitamin D_3 are very high, one of skill in the art would have found it obvious to administer vitamin D orally in humans to treat proton radiation, fluoroscopic radiation, alpha radiation, beta radiation and gamma radiation. This argument is incorrect for two reasons. First, UV radiation has a different wavelength than any of proton radiation, fluoroscopic radiation, alpha radiation, beta radiation and gamma radiation. Thus, a skilled person cannot draw any conclusions regarding the molar absorption coefficient for vitamin D for any of proton radiation, fluoroscopic

radiation, alpha radiation, beta radiation and gamma radiation, from knowledge of the molar absorption coefficient of vitamin D for ultraviolet radiation.

Second, Kita relies on absorption of UV radiation by placement of vitamin D between the radiation and the human, e.g. on the skin. The Examiner has not explained how oral ingestion of vitamin D will place the vitamin D between the radiation and the human so that the vitamin D could absorb the radiation. In actual fact, by the time the radiation reaches the orally ingested vitamin D for absorption, it will have already passed through several organs of the body and have done its damage. Thus, the proposed modification of Kita just won't work since it does not place the vitamin D between the radiation and the body to allow absorption of the radiation prior to the radiation damaging the body.

Thus, the Applicant respectfully requests that the rejections under 35 U.S.C. § 103(a) be withdrawn upon reconsideration.

Claims 5-6 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,162,801, issued to Kita (hereinafter "Kita"), Bissett, D.L. *et al.*, *J. Soc. Cosmet. Chem.* **1992**, *43*, 85-92 (hereinafter "Bissett"), and Darr, D. *et al.*, *British Journal of Dermatology* **1992**, *127*, 247-253 (hereinafter "Darr"), in view of Shimoi, K., *et al.*, *Mutation Research* **1996**, *350*, 153-161 (hereinafter "Shimoi") and U.S. Patent No. 5,776,460, issued to Kim et al. (hereinafter "Kim"), and further in view of Ishida et al. (U.S. Patent no. 5,141,741) or Nguyen et al. (U.S. Patent no. 5,650,137). Applicant respectfully traverses this rejection for the reasons set forth above since neither Ishida nor Nguyen cures the deficiences of the primary references, as set forth above.

In view of the foregoing remarks, Applicant respectfully submits that all of the pending claims are in condition for allowance and respectfully requests a favorable Office Action so indicating.

Respectfully submitted,

Dated: December 13, 2005

Kevin J. Dunleavy
Reg. No. 32,024

KNOBLE YOSHIDA & DUNLEAVY, LLC
Customer No. 21,302
Eight Penn Center, Suite 1350
1628 John F. Kennedy, Jr. Blvd.
Philadelphia, PA 19103
Phone: (215) 599-0600
Fax: (215) 599-0601